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10/529,011	08/02/2005	Ralph Patrick Braun	036481-0165	8838

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EXAMINER	
SHEN, WU CHENG WINSTON	
ART UNIT	**PAPER NUMBER**
1632	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/19/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/529,011	BRAUN, RALPH PATRICK	
	Examiner	Art Unit	
	Wu-Cheng Winston Shen	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 February 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,7-10,12-14,16-19,21 and 26-53* is/are pending in the application.

4a) Of the above claim(s) *19,31-36 and 42-44* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,7-10,12-14,16-18,21,26-30,37-41 and 45-53* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This application 10/529,011 filed on 08/02/2005 is a 371 of PCT/GB03/04218 09/29/2003 which claims benefit of 60/414,089 09/27/2002.

Amendments of claims, and newly added claims 45-53, which are dependent claims of claim 1, filed on 2/20/2007 has been received and entered.

Election/Restriction

1. Applicant's election with traverse of Group I, claims 1-21, 22-25, 26-30, 37, 38, and 39-41, drawn to a nucleic acid construct comprising viral genomic nucleic acid where the viral genomic nucleic acid is (1) (i) herpes virus genomic nucleic acid or (ii) a nucleic acid sequence that has at least 80% sequence homology to a herpes virus genomic nucleic acid, and (2) comprises, said viral genomic nucleic acid comprising at least two endogenous gene expression regulatory units which each comprise an endogenous promoter that is capable of expression in a mammalian cell, where the endogenous promoters of the units are active at the same phase in the herpes viral life cycle, wherein (a) the are each operably linked to a separate coding sequence and (b) the viral genomic nucleic acid is from 1 to 50 kb in length and (c) more than 10% and up to 95% of the viral sequences, which are present in the region of the viral genome corresponding to that between the 5' and 3' ends of the viral genomic nucleic acid in the construct, are absent from the construct (claim 1); a coated particle suitable for delivery from a particle-mediated delivery device, which particles comprises carrier particles coated with a nucleic acid construct of claim 1 (claim 26), and a method of generating a nucleic acid construct for direct administration to a subject to elicit an immune response in the subject, the method comprising

recited a nucleic acid construct of claim 1 (claim 37), in the reply filed on Feb. 20, 2007 is acknowledged. In response to further restriction of claims 5, 6, 7, and 8, Applicants further elect: (i) DNA virus (claim 5); (ii) herpes virus (claim 6); (iii) HSV (claim 7); and (iv) HSV-2 (claim 8).

The traversal is on the ground(s) that **(i)** with respect to HSV-1 and HSV-2, Applicants submitted that they should not have to restrict claim 8 to cover only one of the two subspecies of HSV. Both subspecies of HSV are similar and would not impose any undue search burden on the Examiner. Applicants' invention applies equally to both virus subtypes, **(ii)** with regard to election of species of one ICP gene promoter recited in claims 9 and 11, Applicants stated that one aspect of Applicants' invention is to immunize a subject against a virus by delivering a viral construct into the subject. The viral construct comprises selected fragments from a particular virus genome and, as such, those fragments necessarily contain certain genes, promoters, and regulatory elements that reside in their native genomic context. Thus, a viral genomic fragment may contain multiple native genes and therefore it would necessarily contain multiple native promoters that are naturally linked to their respective genes. One key aspect of the invention, therefore, is a genomic viral fragment that comprises at least two endogenous promoters for driving expression of their respective coding sequences. The presence of at least two endogenous promoters is a feature of all of the original claims. Thus, Applicants respectfully assert for the record that the claimed invention requires two promoters and Applicants make a species election solely to assist the Examiner in his preliminary searches of the claimed invention. Applicants do not hereby in any way limit the claimed invention to only the one elected promoter species. Accordingly, Applicants elected species ICP0 from claim 9 and cancelled claim 11.

The traversal is not found persuasive, with respect to restriction between HSV-1 and HSV-2 recited in claim 8, because, as indicated in the Restriction Requirement, HSV-1 and HSV-2 comprise structurally distinct nucleotide sequences and are distinct chemical components and are unrelated to one another. Furthermore, it is well established the tropism of HSV-1 and HSV-2 are distinct and they cause oral and genital infection respectively. Therefore, claim 8 is examined as HSV being HSV-2. Accordingly, claim 19 reciting HSV-1 is withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim.

With regard to election of species of one of the recited ICP gene promoters in claims 9 and 11, the requirement for election of species between ICP0, ICP4, ICP22, and ICP27 is withdrawn upon further consideration of applicant's traversal of claim 9 and cancellation of claim 11.

In the reply filed on Feb. 20, 2007, Applicants cancelled the claims 5-6, 11, 15, 20, 22-25. Claim 31-36 and 42-44 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim.

The requirement is still deemed proper and is therefore made FINAL.

Status of claims: claims 1-4, 7-10, 12-14, 16-18, 21, 26-30, 37-41, 45-53 are currently under examination.

Claim Objections

2. Claims 26, 27, and 39 are objected to because of the following informalities: There is no article (i.e. "A") in the beginning of these claims. Appropriate correction is required.

Claim Rejection - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

3. Claims 1-4, 7-10, 13-14, 16-19, 21, and 46-53 are rejected under 35 U.S.C. 101 because the claimed invention, independent claim 1, and their dependent claims 2-4, 7-14, 16-19, 21, and 45-53, are directed to a non-statutory subject matter.

Upon broad and reasonable interpretation, the term "a nucleic acid construct" recited in 1 encompass products of nature, for instance a complete or part of herpes virus genomic nucleic acid sequences integrated into a human genome, which is a non-statutory subject matter.

It is noted that the coding sequences recited in claim 12 read on the coding sequences of HSV genes; however, the HSV is not considered as an organism. Therefore, claim 12 is not rejected under 35 U.S.C. 101. Regarding claims 13 and 14, HSV is a pathogen and the products of HSV genes are antigens. Therefore, claims 13 and 14 are rejected under 35 U.S.C. 101.

Amending the claim to an *isolated* nucleic acid composition will obviate the rejection.

Claim Rejection - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

4. Claims 1-4, 7-10, 12-14, 16-19, 21, 26-30, 37-41, 45-53 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The phrase "inserting herpes virus genomic nucleic acid or a sequence with *at least 80% sequence homology* into a vector backbone" recited in claim 37 of instant application is vague and indefinite. It is unclear to what sequences the recited 80% sequence homology is compared. It is noted that there is no sequence of any Herpes virus genomic nucleic acid has been disclosed in the specification of instant application. Claims 38-41 depend from claim 37.

The phrase "where the endogenous promoters of the units are *active at the same phase in the herpes virus life cycle*" recited in claims 1 and 37 of instant application is vague and indefinite. Claims 2-4, 7-10, 12-14, 16-19, 21, 26-30, 38-41, 45-53 depend from claims 1 and 37. It is unclear how the endogenous promoters of the units are the phrase "*active* at the *same phase in the herpes virus life cycle*" is defined. There are two issues encompassed by the stated claim: first, it is unclear that on what basis with regard to expression level, the recited promoter is considered as active; and second, how the recited phase of the herpes virus life cycle is defined. In this regard, the specification only provides the following relevant, but undefined, statements: "The endogenous promoters, to which the heterologous coding sequences are operably linked, will preferably be expressed in the same phase and typically at a similar, or same, time in the viral cycle of the virus the viral genomic nucleic acid is derived from. Viral life cycles are typically divided into phases, each of which may involve the expression of a particular subset of genes, the genes being classified as to what phase they are expressed at. For

example, a viral life cycle may involve immediate early, early and late gene expression or gene expression during a period of latency. Thus in many embodiments the endogenous promoters of the gene expression regulatory units will be those of viral genes from the same or adjacent phases in the viral life cycle and preferably the same phase. Thus they may all be immediate early, early, late or latency associated promoters (See parag. [0092], instant application).

It is noted that claim 1 recites the limitation " *the same* phase" in the 7th line of claim 1. There is insufficient antecedent basis for this limitation in the claim.

5. Claims 3 and 39-41 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 3 recites "expression regulatory units are immediate early genes" is unclear because regulatory units are not equivalent to genes.

Claims 38-41 depend from claim 36, which is a non-elected invention.

6. Claims 14, 16, 17 and 51 are rejected under 35 U.S.C. 112, second paragraph, because there is insufficient antecedent basis for this limitation in the claim.

Claims 14 recite the limitation "*the antigens*" in claim 14 "A nucleic acid construct according to claim 1, wherein the antigens are antigens from a pathogen". There is insufficient antecedent basis for this limitation in the claim.

Claims 16 and 17 recite the limitation "*the absent* region" in line 2 of claims 16 and 17. There is insufficient antecedent basis for this limitation in the claim.

Claim 51 recites the limitation "*the* herpes virus genome" in "at least 90% homology to the endogenous sequences of *the* herpes virus genome". There is insufficient antecedent basis for this limitation in the claim.

Claim Rejection - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1-4, 7-10, 12-14, 16-18, 21, 26-30, 37-41, and 45-53 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

It is noted that there is no sequence of any Herpes virus genomic nucleic acid has been disclosed in the specification of instant application.

The claims are directed a method of producing an isolated nucleic acid molecule, a vector comprising the same nucleic acid molecule as a vector for vaccination, and pharmaceutical compositions comprising the same nucleic acid molecule coated in a particle for delivery into a mammalian cell.

With regard to claims 1-4, 7-10, 12-14, 16-18, 21, 26-30, and 45-53, the nucleotide sequences of Herpes virus genomic nucleic acid, variants, and fragments (including the recited limitation *a nucleic acid sequences that has at least 80% sequence homology to a herpes virus* in

claim1) thereof encompassed within the genus of nucleotide sequences of Herpes virus genomic nucleic acid have not been disclosed. Based upon the prior art there is expected to be variation among the species of Herpes virus genomic nucleic acid sequences, because the Herpes virus genomic nucleic acid sequences would be expected to vary among individual Herpes viruses that target different mammalian host, and among different tissues of a given mammalian host. The specification does not disclose any part of Herpes virus genomic nucleic acid sequences that infect any mammals or other Herpes virus genomic nucleic acid sequences that infect different tissues of a given mammal, or different isolates from the same tissue or cell type of a given mammal. There is no evidence on the record of a relationship between the structure of any Herpes virus genomic nucleic acid sequences and the claimed Herpes virus genomic nucleic acid that would provide any reliable information about the structure of other Herpes virus genomic nucleic acid sequences within the genus. There is no evidence on the record that the asserted Herpes virus genomic nucleic acid had a known structural relationship to any other Herpes virus genomic nucleic acid sequences; the specification discloses none of Herpes virus genomic nucleic acid obtained from any origin; the art indicated that there is variation between Herpes virus genomic nucleic acid sequences and their functions. The specification has not even disclosed the type (or variant) of Herpes virus genomic nucleic acid sequences. In the absence of a functional assay it would not be possible to test variants of the claimed sequences for biological activity. In view of the above considerations one of skill in the art would not recognize that applicant was in possession of the necessary common features or attributes possessed by member of the genus, because no Herpes virus genomic nucleic acid sequences is presented as a representative of the claimed genus. Consequently, since Applicant was not documented in

possession of any Herpes virus genomic nucleic acid sequences and since the art recognized variation among the species of the genus of Herpes virus genomic nucleic acid sequences, the claimed Herpes virus genomic nucleic acid sequences was not considered as a representative of the claimed genus. Therefore, Applicant was not in possession of the genus of Herpes virus genomic nucleic acid sequences as encompassed by the claims. Accordingly, Applicant was not in possession of the even broader genus of "at least 80% sequence homology to a Herpes virus genomic nucleic acid" as encompassed by the claims. University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that to fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention."

Claim Rejection - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 1-4, 7-9, 12-14, 16, 17, 21, 26-30, 37-41, and 45-49 are rejected under 35 U.S.C. 102(b) as being anticipated by Roizman et al. (Roizman, U.S. Patent Number: 5,288,641, issued Feb, 22, 1994) as evidenced by Leopardi et al. (U. S Patent number: 5,876,923, issued Mar. 2, 1999).

It is noted that Roizman and Leopardi et al. disclosed the information encompassed by the claimed invention of the instant application. It is further noted that different interpretations

of claims can be applied to the rejections under 35 U.S.C. 102 and the rejection 35 U.S.C. 112 first paragraph pertaining to enablement issue. Therefore, there is no contradiction between the art rejection stated here and the rejection under 35 U.S.C 112, first paragraph.

Roizman teaches Herpes Simplex virus (HSV), including HSV-1 and HSV-2, as a vector and a foreign gene is inserted into a viral genome under the control of promoter-regulatory regions of the genome, thus providing a vector for the expression of the foreign gene. DNA constructs, plasmid vectors containing the constructs useful for expression of the foreign gene, recombinant viruses produced with the vector, and associated methods are disclosed (See title and abstract, Roizman, 1994).

More specifically, Roizman teach the construction of plasmid pRB3225 (See Fig. 4, columns 6 and 7, claim 14, Roizman, 1994) from pRB3223 (See Fig. 2., columns 4 and 5, claim 13, Roizman, 1994,). The plasmid pRB3225 harbors a chimeric gene $P_{\alpha 4}$-HBsAg cloned into the *Bgl* II site, a non-coding region, of the TK (thymidine kinase) gene. Therefore, the pRB3225 comprises HbsAg (hepatitis B surface antigen) ending sequences driven by the ICP4 promoter (i.e. $P_{\alpha 4}$-HbsAg) of HSV, and the β promoter of the TK gene --- which is encompassed by the limitation of claim 1 regarding the viral genomic nucleic acid being from 1 to 50 kb, and two endogenous gene expression regulatory units.

With regard to the limitation on the endogenous promoter being active at the same phase in the herpes virus life cycle, Roizman further teaches HSV genes form three major groups designated as α, β, and γ, the expression of which is coordinately regulated and sequentially ordered in a cascade fashion. It is known that for most α and some β genes the promoter and regulatory domains are located upstream from the site of initiation of transcription.

Specifically, chimeric genes constructed by fusion of promoter-regulatory domains of α gene (e.g., the gene specifying infected cell protein (ICP) Nos. 0, 4, 27 or 22, which are also known as *immediate early genes* as recited in claim 3 of instant application) to the 5' transcribed non-coding and coding sequences of other genes are regulated as α or β genes, respectively (See lines 8-18, column 3, Roizman, 1994). Therefore, the TK gene (a β group gene, encompassed by early viral gene recited in claim 3 of instant application) and ICP4 gene (an α group gene encompassed by immediate early gene recited in claim 3 of instant application) are active in the same productive replication phase of the herpes virus life cycle at the site of primary infection.

With regard to claim HSV-2 recited in claim 8 of instant application, Roizman teach the DNA of Herpes Simplex virus, type 2, (HSV-2) is essentially identical in structure to that of HSV-1, and differs only in nucleotide matching of base pairs. Therefore, DNA constructs identical to those illustrated herein using the HSV-1 genome are feasible according to the present invention (See lines 38-43, column 9, Roizman, 1994).

With regard to claims 13 and 14 of instant application, Roizman teaches coding sequence of antigens of TK of HSV-1 and HbsAg of Hepatitis B virus.

With regard to claims 16, 17 and 45-49 of instant application, the plasmids pRB3225 and pRB3223 taught by Roizman contain ICP4 promoter and is absent of other genes and intervening sequences of HSV-1 genomic nucleic acid sequences.

With regard to particle-mediated DNA transfer (claims 26-30, and 38-40), it is known in the art that particle mediated DNA transfer can be used in DNA vaccination at the time of filing of instant application. For instance, Leopardi et al. teach the transfer of the construct may be performed by any of the methods that physically or chemically permeabilize the cell membrane.

Several devices for accelerating small particles have been developed. One such device relies on a high voltage discharge to generate an electrical current, which in turn provides the motive force. The microprojectiles used have consisted of biologically inert substances such as tungsten or gold beads (See lines 38-55, column 16, Leopardi et al., 1999)

Thus, Roizman clearly anticipates claims 1-4, 7-9, 12-14, 16, 17, 21, 26-30, 37-41, and 45-49 of instant invention.

Conclusion

9. No claim is allowed.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Any inquiry concerning this communication from the examiner should be directed to Wu-Cheng Winston Shen whose telephone number is (571) 272-3157 and Fax number is 571-273-3157. The examiner can normally be reached on Monday through Friday from 8:00 AM to 4:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the supervisory patent examiner, Peter Paras, can be reached on (571) 272-4517. The fax number for TC 1600 is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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